I. AMENDMENTS

AMENDMENTS TO THE CLAIMS

Cancel claim 3 without prejudice to renewal.

Please enter the amendment to claim 1, as shown below.

1. (Currently amended) A gene-targeted mouse comprising a modified endogenous apolipoprotein E (apoE) allele, wherein said modified allele comprises an apoE-encoding nucleic acid under transcriptional control of endogenous regulatory sequences, wherein the modified allele encodes a modified apoE polypeptide that exhibits domain interaction characteristic of human apolipoprotein E4 (apoE4), wherein the modified apoE polypeptide comprises a Thr → Arg substitution at a position equivalent to amino acid 61 of human apoE4, wherein the gene-targeted mouse is homozygous for the modified apoE allele, and wherein the modified apoE polypeptide exhibits preferential binding to lower density lipoproteins, and wherein the mouse exhibits apoE4-related neurodegeneration.

2.-4. (Canceled)

5. (Previously presented) A cell isolated from the gene-targeted mouse of claim 1, wherein said cell produces the modified apoE polypeptide.

6. (Canceled)

7. (Previously presented) The cell of claim 5, wherein the cell is homozygous for the modified apoE allele.

8.-13. (Canceled)

14. (Currently amended) A method of identifying an agent that reduces apoE4-related neurodegeneration ~~a phenomenon associated with Alzheimer's disease (AD)~~, the method comprising:

a) contacting the gene-targeted mouse of claim 1 with a test agent; and

b) determining the effect of the test agent on reducing apoE4-related neurodegeneration ~~a phenomenon associated with AD~~.

15.-19. (Canceled)

20. (Previously presented) The cell according to claim 5, wherein said cell is an astrocyte.

21. (Previously presented) The cell according to claim 5, wherein said cell is a microglial cell.

22. (Previously presented) The cell according to claim 5, wherein the cell is a neuronal cell.

23. (Canceled)